

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 21

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte LEON W. TERSTAPPEN and CHIA-HUEI CHEN

Appeal No. 1997-2391
Application 08/239,265¹

ON BRIEF

Before ROBINSON, SPIEGEL and SCHEINER, Administrative Patent Judges.
SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 13, 15 and 16, all the claims remaining in the application.

Claims 1, 5, 6 and 8 are representative of the subject matter on appeal and read as follows:

¹ Application for patent filed May 6, 1994. According to appellants, this application is a continuation of Application 07/823,911, filed January 22, 1992, now abandoned.

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Kansas et al. (Kansas), "Expression of the CD11/CD18, Leukocyte Adhesion Molecule 1, and CD44 Adhesion Molecules During Normal Myeloid and Erythroid Differentiation in Humans," Blood, Vol. 76, No. 12, pp. 2483-492 (Dec. 1990)

Claims 1 through 7, 10 through 13, 15 and 16 stand rejected under 35 U.S.C. § 103 as unpatentable over Loken and Kansas. Claims 8 and 9 stand rejected under 35 U.S.C. § 103 as unpatentable over Loken, Kansas and Basch. We reverse both rejections.

DISCUSSION

Claim 1, directed to multi-parameter analysis of cells in body fluid, represents the invention in its broadest aspect: erythrocyte precursors and proliferating cells, among others, are identified and counted based on differential light scatter and differential binding of a fluorescent nucleic acid dye, a first monoclonal antibody specific for an antigen differentially expressed on the cells, and a second monoclonal antibody specific for an antigen differentially expressed on erythrocyte precursors and proliferating cells (the two antibodies have fluorescent labels with peak emission spectra different from each other and from the nucleic acid dye). The two antibodies are described in functional terms in claim 1, but there is no requirement that they recognize any antigen in particular. Nevertheless, both the examiner and appellants have focused throughout the prosecution on that embodiment of the method wherein the first fluorescently-labeled monoclonal antibody is specific for CD45 and the second is specific for CD71 (as required in claims

5, 6, 12, 13, 15 and 16). As this board functions as a board of review, not a de novo examination tribunal, we shall do likewise.²

There are two rejections under 35 U.S.C. § 103, and each is based on the combination of Loken and Kansas. We view the examiner's proposed combination of these two references as the dispositive issue in each of the rejections.

Loken discloses multi-parameter analysis of erythrocytes, reticulocytes, nucleated erythrocytes, platelets, lymphocytes, monocytes, neutrophilic granulocytes, basophilic granulocytes, eosinophilic granulocytes, and precursors of nucleated cells in body fluid (e.g., whole blood or bone marrow aspirates) using two channels of light scatter and differential binding of two fluorescent nucleic acid dyes and at least one fluorescently labeled monoclonal antibody (with different peak emission spectra). In a preferred embodiment, thiazole-orange (an RNA dye), LDS-751 (a DNA dye) and phycoerythrin-labeled anti-CD45 monoclonal antibody are used to identify and count individual cells in a sample. According to appellants, Loken's analysis differs from the claimed analysis in that:

[It] does not permit full discrimination among the erythroid lineage (i.e., it does not permit identification of orthochromatic normoblasts, normoblasts and erythroblasts and does not permit differentiation between mature and immature reticulocytes) and does not permit the identification of proliferating

² 35 U.S.C. § 6(b): "The [board] shall . . . review adverse decisions of examiners upon applications for patents"

myeloid cells and non-hematopoietic cells (i.e., stromal and epithelial cells). (Specification, page 2).

Kansas describes the pattern of expression of three classes of leukocyte adhesion molecules during normal differentiation of monocytes, granulocytes, and erythrocytes in humans: the CD11/CD18 heterodimers (including CD11a/CD18, the leukocyte function-associated antigen 1 (LFA-1)), the CD44 family, and the LAM-1 (leukocyte adhesion molecule 1) molecule(s). Differential expression of transferrin receptor/CD71 and CD45 was noted in the course of investigating the down regulation of CD44 during erythroid development:

Although the absence of any markers specific for glycoG erythroid cells make analysis of the phenotype of these cells difficult, the data described below indirectly suggest that these early committed erythroid cells are CD44^{hi}LFA-1GLAM-1G. No cells coexpressing glyco and either LFA-1 or LAM-1 were detectable . . . , consistent with the loss of these markers being an early event in erythropoiesis. In contrast, CD44 was expressed at high levels on a subset of glyco⁺ cells; further analysis showed that these glyco⁺CD44^{hi} cells coexpressed CD45, a marker found on all leukocytes and early erythroid cells. Glyco⁺ cells that expressed intermediate levels of CD44 were transferrin receptor/CD71⁺. Glyco⁺ cells expressing neither CD45 nor CD71 expressed low levels of CD44, similar to that found on normal, circulating RBC. Thus, CD44 expression declines gradually in a stepwise fashion during normal erythropoiesis. (Kansas, page 2486, citations and references to figures omitted).

In addition, Figure 4b of Kansas shows that “most glyco⁺CD71⁺ cells are CD44^{int}, but a minor subset of the glyco⁺CD71⁺ are CD44^{hi}.”

The examiner believes that it would have been obvious to combine anti-CD45 and anti-CD71 monoclonal antibodies in Loken's method because "[Loken] teach[es] the combination of nucleic acid dyes and anti-CD45 as providing a distinction between only mature erythrocytes and reticulocytes, and not identifying earlier precursors to the erythrocytes" while "[Kansas] teach[es] antibodies to CD71 in combination with anti-CD45 as providing a means of distinguishing erythroid precursors and proliferating cells" (Office Action mailed December 13, 1994, Paper No. 14).

We do not agree. As appellants point out, Kansas focuses on expression of three specific leukocyte adhesion molecules (CD11/CD18, LAM-1 and CD44) during normal myeloid and erythroid differentiation (Brief, page 6). The appearance and subsequent disappearance of CD71 and CD45 during erythropoiesis are mentioned in passing, and then only in the larger context of the gradual, stepwise decline in CD44 expression during erythropoiesis. While one would recognize from Kansas that CD71 and CD45 are differentially expressed during erythropoiesis, the discussion of their occurrence at various stages of cell maturity is fragmentary, especially in comparison with the discussion of CD44 expression. It is only with the use of impermissible hindsight that Kansas can be considered to suggest CD71 and CD45 expression patterns as "a means of distinguishing erythroid precursors and proliferating cells."

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We have no doubt that the prior art could be modified in the manner proposed by the examiner, but the fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Here, we find no reason stemming from the prior art which would have led a person having ordinary skill to the claimed invention. In our judgment, the only reason or suggestion to combine the references in the manner proposed by the examiner comes from appellants' specification. Accordingly, we reverse the rejections of claims 1 through 7, 10 through 13, 15 and 16 under 35 U.S.C. § 103.

In addition to Loken and Kansas, the examiner relies on Basch in rejecting claims 8 and 9 under 35 U.S.C. § 103. Basch does not remedy the underlying

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deficiency in the examiner's conclusion of obviousness. The rejection of claims 8 and 9 under 35 U.S.C. § 103 is reversed as well.

REVERSED

DOUGLAS W. ROBINSON)
Administrative Patent Judge

CAROL A. SPIEGEL
Administrative Patent Judge

TONI R. SCHEINER)
Administrative Patent Judge

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